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NEWS	2		"Ask CAS" for self-help around the clock
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NEWS	5	AUG 02	CAplus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS	6	AUG 02	The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS	7	AUG 27	BIOCOMMERCE: Changes and enhancements to content coverage
NEWS	8	AUG 27	BIOTECHABS/BIOTECHDS: Two new display fields added for legal status data from INPADOC
NEWS	9	SEP 01	INPADOC: New family current-awareness alert (SDI) available
NEWS	10	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	11	SEP 01	New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS	12	SEP 27	STANDARDS will no longer be available on STN
NEWS	13	SEP 27	SWETSCAN will no longer be available on STN

NEWS EXPRESS	JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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FILE 'HOME' ENTERED AT 12:42:48 ON 26 OCT 2004

=> File caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 12:42:54 ON 26 OCT 2004

FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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=> "multiplicity of infection" (s) definition
          24055 "MULTIPLICITY"
           4978 "MULTIPLICITIES"
          27034 "MULTIPLICITY"
                  ("MULTIPLICITY" OR "MULTIPLICITIES")
              0 "OF"
            164 "OFS"
            164 "OF"
                  ("OF" OR "OFS")
         213259 "INFECTION"
          64280 "INFECTIONS"
         245413 "INFECTION"
                  ("INFECTION" OR "INFECTIONS")
              0 "MULTIPLICITY OF INFECTION"
                  ("MULTIPLICITY"(W)"OF"(W)"INFECTION")
          36378 DEFINITION
           8470 DEFINITIONS
          43306 DEFINITION
                  (DEFINITION OR DEFINITIONS)
L1            0 "MULTIPLICITY OF INFECTION" (S) DEFINITION

=> "multiplicity of infection" (l) definition
          24055 "MULTIPLICITY"
           4978 "MULTIPLICITIES"
          27034 "MULTIPLICITY"
                  ("MULTIPLICITY" OR "MULTIPLICITIES")
              0 "OF"
            164 "OFS"
            164 "OF"
                  ("OF" OR "OFS")
         213259 "INFECTION"
          64280 "INFECTIONS"
         245413 "INFECTION"
                  ("INFECTION" OR "INFECTIONS")
              0 "MULTIPLICITY OF INFECTION"
                  ("MULTIPLICITY"(W)"OF"(W)"INFECTION")
          36378 DEFINITION
           8470 DEFINITIONS
          43306 DEFINITION
                  (DEFINITION OR DEFINITIONS)
L2            0 "MULTIPLICITY OF INFECTION" (L) DEFINITION
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=> "Multiplicity of infection" and definition
         24055 "MULTIPLICITY"
          4978 "MULTIPLICITIES"
         27034 "MULTIPLICITY"
                 ("MULTIPLICITY" OR "MULTIPLICITIES")
             0 "OF"
           164 "OFS"
           164 "OF"
                 ("OF" OR "OFS")
        213259 "INFECTION"
         64280 "INFECTIONS"
        245413 "INFECTION"
                 ("INFECTION" OR "INFECTIONS")
             0 "MULTIPLICITY OF INFECTION"
                 ("MULTIPLICITY"(W)"OF"(W)"INFECTION")
         36378 DEFINITION
          8470 DEFINITIONS
         43306 DEFINITION
                 (DEFINITION OR DEFINITIONS)
L3           0 "MULTIPLICITY OF INFECTION" AND DEFINITION

=> multiplicity (s) infection
         24055 MULTIPLICITY
          4978 MULTIPLICITIES
         27034 MULTIPLICITY
                 (MULTIPLICITY OR MULTIPLICITIES)
        213259 INFECTION
         64280 INFECTIONS
        245413 INFECTION
                 (INFECTION OR INFECTIONS)
L4        1987 MULTIPLICITY (S) INFECTION

=> HIV
         57099 HIV
            89 HIVS
L5       57113 HIV
                 (HIV OR HIVS)

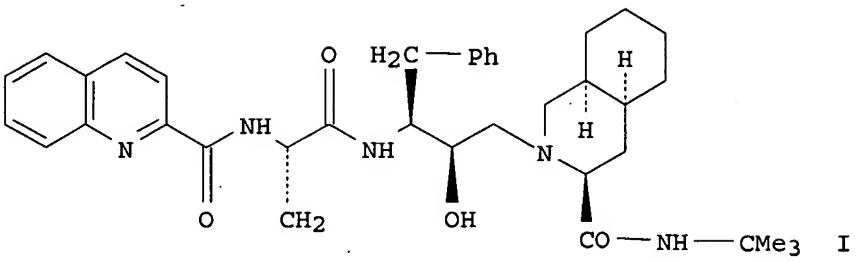
=> L4 and L5
L6         121 L4 AND L5

=> dosage and L6
        119114 DOSAGE
         17784 DOSAGES
        132237 DOSAGE
                 (DOSAGE OR DOSAGES)
L7           1 DOSAGE AND L6

=> D L7 IBIB ABS

L7   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         1994:645184  CAPLUS
DOCUMENT NUMBER:          121:245184
TITLE:                    Long-term treatment of HIV-infected MT-4
                          cells in culture with HIV proteinase
                          inhibitor Ro 31-8959 leads to complete cure of
                          infection
AUTHOR(S):                Nitschko, H.; Lindhofer, H.; Schaetzl, H.; Eberle, J.;
                          Deby, G.; Kranz, B.; von der Helm, K.
CORPORATE SOURCE:         Max-von-Pattenkofer Inst., Univ. Munich, Munich,
                          D-80336, Germany
SOURCE:                   Antiviral Chemistry & Chemotherapy (1994), 5(4),
                          236-42
                          CODEN: ACCHEH; ISSN: 0956-3202
```

DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB An **HIV**-infected cell culture was treated with the specific **HIV** proteinase inhibitor Ro 31-8959 (I) for three months to analyze the antiviral effect and possible cytotoxicity of the drug in long-term treatment. The drug was added 1 h after **HIV** **infection** with 0.002 **multiplicity** of **infection** and maintained for 87 days in the cell culture. There was no detectable cell death nor any evidence of **HIV** production in this time. Cells were proven to be initially infected, since premature drug removal led to a re-emergence of infectious **HIV** and cell death. However, after 87 days of treatment the drug could be removed safely and **HIV** was cleared demonstrably from the culture. These data suggest that long-term **dosage** may be advantageous to the clin. treatment of **HIV** infection by **HIV** proteinase inhibitors.

=> titer and L6
23398 TITER
20743 TITERS
40306 TITER
(TITER OR TITERS)
L8 12 TITER AND L6

=> D L8 IBIB ABS 1-12

L8 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:341053 CAPLUS
DOCUMENT NUMBER: 140:117094
TITLE: Multiply Attenuated, Self-Inactivating Lentiviral Vectors Efficiently Deliver and Express Genes for Extended Periods of Time in Adult Rat Cardiomyocytes In Vivo
AUTHOR(S): Fleury, Sylvain; Simeoni, Eleonora; Zuppinger, Christian; Deglon, Nicole; von Segesser, Ludwig K.; Kappenberger, Lukas; Vassalli, Giuseppe
CORPORATE SOURCE: Division of Cardiology, University of Lausanne, Lausanne, Switz.
SOURCE: Circulation (2003), 107(18), 2375-2382
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Among retroviral vectors, lentiviral vectors are unique in that they transduce genes into both dividing and nondividing cells. However, their ability to provide sustained myocardial transgene expression was not evaluated. Multiply attenuated, self-inactivating lentivectors based on human immunodeficiency virus-1 contained the enhanced green fluorescent protein (EGFP) gene under the transcriptional control of either the

cytomegalovirus (CMV) immediate-early enhancer/promoter, the elongation factor-1α (EF-1α) promoter, or the phosphoglycerate-kinase (PGK) promoter. Lentivectors transduced adult rat cardiomyocytes in a dose-dependent manner (transduction rate,>90%; **multiplicity** of **infection**,≈5). The CMV promoter achieved higher EGFP expression levels than the EF-1α and PGK promoters. Insertion of the central polypurine tract pol sequence improved gene transfer efficiency by ≈2-fold. In vivo gene transfer kinetics was studied by measuring the copy number of integrated lentivirus DNA and EGFP concns. in cardiac exts. by real-time polymerase chain reaction and ELISA, resp. With CMV promoter-containing lentivectors, vector DNA peaked at day 3, declined by ≈4-fold at day 14, but then remained stable up to week 10. Similarly, EGFP expression peaked at day 7, decreased by ≈7-fold at day 14, but was essentially stable thereafter. In contrast, vector DNA and EGFP expression with **titer**-matched adeno-vectors was ≈35% higher than with CMV lentivectors but was lost rapidly over time. Lentivectors efficiently transduce and express genes for extended periods of time in cardiomyocytes in vivo. Lentivectors provide a useful tool for studying myocardial biol. and a potential system for gene heart therapy.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:199208 CAPLUS

DOCUMENT NUMBER: 137:74156

TITLE: Transduction of human PBMC-derived dendritic cells and macrophages by an **HIV**-1-based lentiviral vector system

AUTHOR(S): Schroers, Roland; Sinha, Indu; Segall, Harry; Schmidt-Wolf, Ingo G. H.; Rooney, Cliona M.; Brenner, Malcolm K.; Sutton, Richard E.; Chen, Si-Yi

CORPORATE SOURCE: Center for Cell and Gene Therapy, Department of Pediatrics, Baylor College of Medicine, Houston, TX, 77030, USA

SOURCE: Molecular Therapy (2000), 1(2), 171-179
CODEN: MTOHCK; ISSN: 1525-0016

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Professional antigen-presenting cells, such as dendritic cells (DCs) and macrophages, are target cells for gene therapy of infectious disease and cancer. However, transduction of DCs and macrophages has proved difficult by most currently available gene transfer methods. Several recent studies have shown that lentiviral vector systems can efficiently transduce many nondividing and differentiated cell types. In this study, we examined the gene transfer to DCs and macrophages using a lentiviral vector system. Human DCs were propagated from the adherent fraction of peripheral blood mononuclear cells (PBMCs) by culture in medium containing GM-CSF, IL-4, and TNF-α. Human macrophages were propagated from adherent PBMCs in medium containing GM-CSF. High **titers** of a replication-defective vesicular stomatitis virus glycoprotein G pseudotyped **HIV** -1-based vector encoding the enhanced yellow fluorescent protein were produced. In immature DCs (culture days 3 and 5), transduction efficiencies of 25 to 35% were achieved at a **multiplicity** of **infection** of 100. However, the transduction efficiency was decreased in more mature DCs (culture day 8 or later). Furthermore, monocyte-derived macrophages were also transduced by the lentiviral vector system. In addition, Alu-LTR PCR demonstrated the integration of the **HIV**-1 provirus into the cellular genome of the transduced DCs and macrophages. Allogeneic mixed lymphocyte reactions revealed similar antigen-presenting functions of untransduced and lentivirally transduced DCs. Thus, the results of this study demonstrate that both PBMC-derived DCs and macrophages can be transduced by lentiviral vectors. (c) 2000

Academic Press.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:211589 CAPLUS
DOCUMENT NUMBER: 134:352197
TITLE: DNA-dependent protein kinase is not required for efficient lentivirus integration
AUTHOR(S): Baekelandt, Veerle; Claeys, Anje; Cherepanov, Peter; De Clercq, Erik; De Strooper, Bart; Nuttin, Bart; Debyser, Zeger
CORPORATE SOURCE: Laboratory for Experimental Neurosurgery and Neuroanatomy, Katholieke Universiteit Leuven, Louvain, Belg.
SOURCE: Journal of Virology (2000), 74(23), 11278-11285
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB How DNA is repaired after retrovirus integration is not well understood. DNA-dependent protein kinase (DNA-PK) is known to play a central role in the repair of double-stranded DNA breaks. Recently, a role for DNA-PK in retroviral DNA integration has been proposed. Reduced transduction efficiency and increased cell death by apoptosis were observed upon retrovirus infection of cultured scid cells. We have used a human immunodeficiency virus (**HIV**) type 1 (**HIV**-1)-derived lentivirus vector system to further investigate the role of DNA-PK during integration. We measured lentivirus transduction of scid mouse embryonic fibroblasts (MEF) and xrs-5 or xrs-6 cells. These cells are deficient in the catalytic subunit of DNA-PK and in Ku, the DNA-binding subunit of DNA-PK, resp. At low vector **titers**, efficient and stable lentivirus transduction was obtained, excluding an essential role for DNA-PK in lentivirus integration. Likewise, the efficiency of transduction of **HIV**-derived vectors in scid mouse brain was as efficient as that in control mice, without evidence of apoptosis. We observed increased cell death in scid MEF and xrs-5 or xrs-6 cells, but only after transduction with high vector **titers** (**multiplicity** of **infection** [MOI], >1 transducing unit [TU]/cell) and subsequent passage of the transduced cells. At an MOI of <1 TU/cell, however, transduction efficiency was even higher in DNA-PK-deficient cells than in control cells. The data suggest a protective role of DNA-PK against cellular toxicity induced by high levels of retrovirus integrase or integration. Another candidate cellular enzyme that has been claimed to play an important role during retrovirus integration is poly(ADP-ribose) polymerase (PARP). However, no inhibition of lentivirus vector-mediated transduction or **HIV**-1 replication by 3-methoxybenzamide, a known PARP inhibitor, was observed In conclusion, DNA-PK and PARP are not essential for lentivirus integration.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:606855 CAPLUS
DOCUMENT NUMBER: 131:298713
TITLE: Proteolytic activity in infected and noninfected insect cells: degradation of **HIV**-1 Pr55gag particles
AUTHOR(S): Cruz, Pedro E.; Martins, Pedro C.; Alves, Paula M.; Peixoto, Cristina C.; Santos, Helena; Moreira, Jose L.; Carrondo, Manuel J. T.
CORPORATE SOURCE: IBET/ITQB, Instituto de Biologia Experimental e Tecnologica/Instituto de Tecnologia Quimica e Biologica, Oeiras, P-2780, Port.

SOURCE: Biotechnology and Bioengineering (1999), 65(2), 133-143
CODEN: BIBIAU; ISSN: 0006-3592
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this work, the proteolytic activity in the supernatant and inside insect cells in culture was evaluated for different **multiplicities** of **infection** (MOI) and times of **infection** (TOI). Several methods to detect proteolytic activity in insect cells were tested and that using fluorescein thiocyanite-casein as a substrate was chosen. It was observed that infection caused not only a reduction in the concentration of proteases by decreasing their synthesis but also an inhibition of the intracellular proteolytic activity by increasing the intracellular ATP level (measured by in vivo NMR, NMR). The maximum proteolytic activity in the supernatant was observed at 72 hpi except when the cells were infected in the late exponential growth phase or with very low MOI, yielding a nonsynchronous infection. The proteolytic degradation of Pr55gag particles was studied during culture and after harvest. In this particular case, it was concluded that the supernatant should be stored at low temperature or quickly purified, since the degradation after 24 h is only 3% at 4°C while at 27°C this value rises to 23%. There is a complex relationship between MOI, TOI, proteolytic activity, and product **titer** and quality. Thus, the optimal conditions for each case will be a compromise between the final product **titer**, the desired product quality, and operational issues like process time and capacity, requiring proper integration between bioreaction and downstream processing.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:105707 CAPLUS
DOCUMENT NUMBER: 128:203982
TITLE: Productive human immunodeficiency virus-1 infection of purified megakaryocytic progenitors/precursors and maturing megakaryocytes
AUTHOR(S): Chelucci, C.; Federico, M.; Guerriero, R.; Mattia, G.; Casella, I.; Pelosi, E.; Testa, U.; Mariani, G.; Hassan, H. J.; Peschle, C.
CORPORATE SOURCE: Departments of Hematology-Oncology and Virology, Istituto Superiore di Sanit, Rome, Italy
SOURCE: Blood (1998), 91(4), 1225-1234
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have evaluated the susceptibility to human immunodeficiency virus (**HIV**)-1 **infection** of in vitro grown megakaryopoietic progenitors/precursors and maturing megakaryocytes (MKs), based on the following approach: (1) human hematopoietic progenitor cells (HPCs), stringently purified from peripheral blood and grown in serum-free liquid suspension culture supplemented with thrombopoietin (Tpo), generated a relatively large number of ≥ 98% to 99% pure megakaryocytic precursors and then mature-terminal MKs; (2) at different days of culture (ie, 0, 5, 8, 10) the cells were inoculated with 0.1 to 1.0 **multiplicity** of **infection** (m.o.i.) of the lymphotropic NL4-3 or 0.1 m.o.i. of the monocytotropic BaL-1 **HIV**-1 strain; (3) finally, the presence of viral mRNA and proteins was analyzed by reverse transcriptase-polymerase chain reaction (RT-PCR)/in situ hybridization and antigen capture assays, resp., on day 2 to 12 of culture. MKs derived from day 0 and day 5 BaL-1-challenged cells do not support viral replication as assessed by p24 ELISA and RT-PCR. On the contrary, **HIV** transcripts and proteins

were clearly detected in all NL4-3 infection expts. by RT-PCR and p24 assay, resp., with the highest viral expression in day 5 to 8 challenged MKs. In situ hybridization studies indicate that the percentage of **HIV**+MKs varies from at least 1% and 5% for day 0 and day 5 infected cells, resp. Production of an infectious viral progeny, evaluated by the capability of culture supernatants from day 5 NL4-3-challenged MKs to infect C8166 T-lymphoblastoid cell line, was consistently observed (viral **titer**, ≈ 5+103 tissue culture infectious dose50/mL/106 cells). Exposure of MKs to saturating concentration of anti-CD4 OKT4A monoclonal antibody (MoAb), which recognizes the CD4 region binding with the gp120 envelope glycoprotein, markedly inhibited **HIV** infection, as indicated by a reduction of p24 content in the supernatants: because the inhibitory effect was incomplete, it is apparent that the infection is only partially CD4-dependent, suggesting that an alternative mechanism of viral entry may exist. Morphol. anal. of day 12 MKs derived from HPCs infected at day 0 showed an impaired megakaryocytic differentiation/maturation: the percentage of mature MKs was markedly reduced, in that ≈ 80% of cells showed only one nuclear lobe and a pale cytoplasm with few granules. Conversely, megakaryocytic precursors challenged at day 5 to 8 generated fully mature day 10 to 12 MKs showing multiple nuclear segmentation. Thus, the inhibitory effect of **HIV** on the megakaryopoietic gene program relates to the differentiation stage of cells subjected to the viral challenge. Finally, HPCs treated with 20 or 200 ng/mL of recombinant Tat protein, analyzed at different days of culture, showed an impaired megakaryocytopoiesis comparable to that observed in **HIV**-infected cells, thus suggesting that Tat is a major mediator in the above described phenomena. These results shed light on the pathogenesis of **HIV**-related thrombocytopenia; furthermore, they provide a model to investigate the effects of **HIV** on megakaryocytic differentiation and function.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:308686 CAPLUS
DOCUMENT NUMBER: 127:12898
TITLE: A new reporter cell line to monitor **HIV** infection and drug susceptibility in vitro
AUTHOR(S): Gervaix, Alain; West, Daniel; Leoni, Lorenzo M.; Richman, Douglas D.; Wong-Staal, Flossie; Corbeil, Jacques
CORPORATE SOURCE: Dep. Med., Univ. California San Diego, La Jolla, CA, 92093-0679, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(9), 4653-4658 CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Determination of **HIV** infectivity in vitro and its inhibition by antiretroviral drugs by monitoring reduction of production of p24 antigen is expensive and time consuming. Such assays also do not allow accurate quantitation of the number of infected cells over time. To develop a simple, rapid, and direct method for monitoring **HIV** infection, we generated a stable T-cell line (CEM) containing a plasmid encoding the green fluorescent protein (humanized S65T GFP) driven by the **HIV**-1 long terminal repeat. Clones were selected that displayed low constitutive background fluorescence, but a high level of GFP expression upon infection with **HIV**. **HIV**-1 infection induced a 100- to 1,000-fold increase in relative fluorescence of cells over 2 to 4 days as monitored by fluorescence microscopy, cytofluorimetry, and flow cytometry. Addition of inhibitors of reverse transcriptase, protease, and other targets at different **multiplicities** of **infection**

permitted the accurate determination of drug susceptibility. This technique also
permitted quantitation of infectivity of viral prepns. by assessment of number of cells infected in the first round of infection. In conclusion, the CEM-GFP reporter cell line provides a simple, rapid, and direct method for monitoring **HIV** infectivity **titers** and antiretroviral drug susceptibility of syncytium-inducing strains.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:153202 CAPLUS
DOCUMENT NUMBER: 126:224185
TITLE: Desialylation of peripheral blood mononuclear cells promotes growth of **HIV**-1
AUTHOR(S): Stamatos, Nicholas M.; Gomatos, Peter J.; Cox, Josephine; Fowler, Arnold; Dow, Nancy; Wohlhieter, John A.; Cross, Alan S.
CORPORATE SOURCE: Division of Retrovirology, Walter Reed Army Institute of Research, Washington, DC, 20307-5100, USA
SOURCE: Virology (1997), 228(2), 123-131
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Activation of peripheral blood CD4+ helper T lymphocytes establishes a permissive state for growth of **HIV**-1. Activated T lymphocytes expressed increased sialidase (neuraminidase) activity and were hyposialylated. Treatment of freshly isolated peripheral blood mononuclear cells (PBMCs) with microbial neuraminidase (NANase) or phytohemagglutinin (PHA) prior to **infection** at low **multiplicity** with T cell line-adapted **HIV**-1IIIB resulted in production of large amts. of p24 antigen and reverse transcriptase. In contrast, neither viral component was detected in the medium of mock-treated cells infected at a similar multiplicity through 21 days in culture. The **titer** of a stock solution of **HIV**-1IIIB was 1.4±0.18 log10 greater in NANase-treated PBMCs than in mock-treated cells; the **titer** was similarly raised 1.5 to 1.76±0.18 log10 in PHA-treated cells. Growth of the primary isolate **HIV** -191/US/OSB was also enhanced in NANase-treated PBMCs; the **titer** of a stock solution of **HIV**-191/US/OSB was 1.0±0.16 log10 greater in NANase-treated PBMCs than in mock-treated cells 7 days after infection. No enhancement of viral growth in PBMCs was detected when NANase was heat-inactivated or specifically inhibited with 2,3-dehydro-2-desoxy-N-acetyl-neuraminic acid prior to use. Treatment of PBMCs with NANase did not alter the distribution of lymphocyte subsets nor change the d. of CD4 antigen per cell after 7 days in culture. Whereas PHA treatment of PBMCs was mitogenic, pretreatment with NANase was not; the amount of [3H]thymidine incorporated into DNA and culture growth characteristics were similar for NANase- and mock-treated cells. Thus, desialylation of PBMCs promoted a permissive state for growth of **HIV**-1 without affecting the rate of DNA synthesis or relative number of target CD4+ cells.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:122004 CAPLUS
DOCUMENT NUMBER: 126:197324
TITLE: Phenotypically Vif- human immunodeficiency virus type 1 is produced by chronically infected restrictive cells
AUTHOR(S): Bouyac, Michele; Rey, Francoise; Nascimbeni, Michelina; Courcoul, Marianne; Sire, Josephine; Blanc, Dominique; Clavel, Francois; Vigne, Robert; Spire,

Bruno
CORPORATE SOURCE: INSERM U372, Marseille, 13276, Fr.
SOURCE: Journal of Virology (1997), 71(3), 2473-2477
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The permissivity of CD4+ transformed T cells for the replication of human immunodeficiency virus type 1 (**HIV**-1) vif mutants varies widely between different cell lines. Mutant vif-neg. viruses propagate normally in permissive CD4+ cell lines but are unable to establish a productive infection in restrictive cell lines such as H9. As a consequence, elucidation of the function of Vif has been considerably hampered by the inherent difficulty in obtaining a stable source of authentically replication-defective vif-neg. viral particles produced by restrictive cells. Vif-Neg., vpr-neg. **HIV**-1 strain NDK stock, produced by the permissive SupT1 cell line, was used to infect restrictive H9 cells. By using a high **multiplicity**, **infection** of H9 cells was achieved, leading to persistent production of viral particles displaying a dramatically reduced infectious virus **titer** when measured in a single-cycle infectivity assay. Although these viral particles were unable to further propagate in H9 cells, they could replicate normally in CEM and SupT1 cells. Comparison of unprocessed and processed Gag proteins in the persistently produced vif-neg. viral particles revealed no defect in the processing of polypeptide precursors, with no inversion of the Pr55gag/p24 ratio. In addition, there was no defect in Env incorporation for the vif-neg. viral particles. Despite their apparently normal protein content, these particles were morphol. abnormal when examined by transmission electron microscopy, displaying a previously described abnormally condensed nucleoid. Chronically infected restrictive cell lines producing stable levels of phenotypically vif-neg. **HIV**-1 particles could prove particularly useful in further studies on the function of Vif in the virus life cycle.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:171400 CAPLUS
DOCUMENT NUMBER: 124:222082
TITLE: High-efficiency gene transfer into CD34+ cells with a human immunodeficiency virus type 1-based retroviral vector pseudotyped with vesicular stomatitis virus envelope glycoprotein G
AUTHOR(S): Akkina, Ramesh K.; Walton, Raquel M.; Chen, Meng Liang; Li, Qi-Xiang; Planelles, Vicente; Chen, Irvin S. Y.
CORPORATE SOURCE: Department Pathology, Colorado State University, Fort Collins, CO, 80523, USA
SOURCE: Journal of Virology (1996), 70(4), 2581-5
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Currently, amphotropic retroviral vectors are widely used for gene transfer into CD34+ hematopoietic progenitor cells. The relatively low level of transduction efficiency associated with these vectors in human cells is due to low viral **titers** and limitations in concentrating the virus because of the inherent fragility of retroviral envelopes. A human immunodeficiency virus type 1 (**HIV**-1)-based retroviral vector containing the firefly luciferase reporter gene can be pseudotyped with a broad-host-range vesicular stomatitis virus envelope glycoprotein G (VSV-G). Higher-efficiency gene transfer into CD34+ cells was achieved with a VSV-G pseudotyped **HIV**-1 vector than with a vector packaged in an amphotropic envelope. Concentration of virus without loss of

viral infectivity permitted a higher **multiplicity** of **infection**, with a consequent higher efficiency of gene transfer, reaching 2.8 copies per cell. These vectors also showed remarkable stability during storage at 4° for a week. In addition, there was no significant loss of **titer** after freezing and thawing of the stock virus. The ability of VSV-G-pseudotyped retroviral vectors to achieve a several-fold increase in levels of transduction into CD34+ cells will allow high-efficiency gene transfer into hematopoietic progenitor cells for gene therapy purposes. Furthermore, since it has now become possible to infect CD34+ cells with pseudotyped **HIV**-1 with a high level of efficiency in vitro, many important questions regarding the effect of **HIV**-1 on lineage-specific differentiation of hematopoietic progenitors can now be addressed.

L8 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:33206 CAPLUS
DOCUMENT NUMBER: 112:33206
TITLE: Expression of antisense RNA fails to inhibit influenza virus replication
AUTHOR(S): Leiter, Josef M. E.; Krystal, Mark; Palese, Peter
CORPORATE SOURCE: Dep. Microbiol., Mt. Sinai Sch. Med., New York, NY, 10029-6574, USA
SOURCE: Virus Research (1989), 14(2), 141-59
CODEN: VIREDF; ISSN: 0168-1702
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cell lines were constructed which permanently express influenza virus-specific RNA. Two approaches were followed. C127 cells were transformed with bovine papilloma virus (BPV) vectors and the resulting cell lines inhibited the replication of influenza virus at low **multiplicity** of **infection** (MOI 0.05). However, examination of cellular RNA using single-stranded probes revealed the presence of both (+)sense and antisense RNA transcripts (45-70 copies/cell). In this BPV-based system the inhibitory activity appeared to be associated with a nonspecific, interferon (IFN)-mediated effect. In the 2nd approach, an expression system was used which involved 293 cells, a chimeric human cytomegalovirus (CMV)/human immunodeficiency virus (**HIV**) promoter, and methotrexate-mediated gene amplification. Cells expressed ≤7500 copies of influenza virus-specific RNA/cell at a steady state level. In this system no RNA transcripts of the copposite orientation were found. However, all cell lines permanently expressing either (-)sense or (+)sense viral RNA failed to reduce influenza virus **titers** in a multi-cycle replication experiment (MOI 0.01).

L8 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:630452 CAPLUS
DOCUMENT NUMBER: 111:230452
TITLE: Infection of brain cells by diverse human immunodeficiency virus isolates: role of CD4 as receptor
AUTHOR(S): Weber, Jonathan; Clapham, Paul; McKeating, Jane; Stratton, Michael; Robey, Ellen; Weiss, Robin
CORPORATE SOURCE: Inst. Cancer Res., Chester Beatty Lab., London, SW3 6JB, UK
SOURCE: Journal of General Virology (1989), 70(10), 2653-60
CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cell lines originally derived from malignant tumors of the brain were infected by diverse human immunodeficiency virus types 1 and 2 (**HIV**-1 and **HIV**-2) isolates. By surface immunofluorescence it was shown that susceptible cells did not bear the CD4 antigen. They were also non-permissive for the formation of plaques by vesicular stomatitis virus pseudotypes and did not form syncytia with

HIV-producing cells. Virus production was of low **titer**, and reverse transcriptase and the p24 antigen were consistently undetectable in the culture supernatants. Output virus could be detected by cocultivation with a sensitive T cell line, C8166, by the culture of supernatant medium with T cells and by detection of proviral **HIV** DNA after amplification. A higher **multiplicity** of input virus was required to establish a brain cell **infection** than was required for T lymphocytes or monocytes. Some **HIV**-susceptible brain cells contained mRNA for CD4 but infection was not blocked by anti-CD4 antibodies. Apparently, **HIV** infection of these cells does not involve CD4 as the cellular receptor.

L8 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:546204 CAPLUS
DOCUMENT NUMBER: 111:146204
TITLE: Susceptibility of human immunodeficiency virus to antiviral agents measured by infectious virus yield reduction
AUTHOR(S): Dianzani, F.; Capobianchi, M. R.; Antonelli, G.; Amicucci, P.; De Marco, F.
CORPORATE SOURCE: Inst. Virol., Univ. Rome, Rome, 00185, Italy
SOURCE: Antiviral Research (1989), 11(5-6), 299-305
CODEN: ARSRDR; ISSN: 0166-3542
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Under single growth cycle conditions in C8166 lymphoblastoid cells human immunodeficiency virus shows a replication curve which is completed in 24 h post-infection. At lower **multiplicity** of **infection** virus yield peaks at .apprx.72 h post-**infection** but in both cases the **titer** of the virus released in the medium is negligible with respect to that which remains cell-associated A method based on back-titration of virus in cryolyzates of C8166 cells infected with **HIV** and treated with antiviral compds. was used to evaluate **HIV** sensitivity to such agents. Under single growth cycle conditions dose-response curves appear linear and permit rapid and accurate determination of the endpoint activity. Under multiple growth cycle conditions the inhibitory activity may be measured during the exponential growth phase, at 48 h post-infection. This method, which directly measures production of infectious virus rather than indirect probes of viral replication such as reverse transcriptase or antigen production, offers the advantage of a precise determination of the degree of activity of antivirals also acting on viral assembly or release. The method was tested using 3'-azido-2',3'-dideoxythymidine, 2',3'-dideoxycytidine, and methylisoprinosine as antiviral agents.

= => EIAV or "equine infectious anemia virus"
L1 1210 EIAV OR "EQUINE INFECTIOUS ANEMIA VIRUS"

=> mutation or mutated (l) L1
L2 516985 MUTATION OR MUTATED (L) L1

=> S2 and L2
L3 846 S2 AND L2

=> "redundant stop codes"
L4 0 "REDUNDANT STOP CODES"

=> deletion (L) L3
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'DELETION (L) L7'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'DELETION (L) L8'
L5 158 DELETION (L) L3

=> "stop codon" (l) L5
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'CODON" (L) L13'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'CODON" (L) L14'
L6 15 "STOP CODON" (L) L5

=> "two mutations" (l) L3
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'UTATIONS" (L) L7'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'UTATIONS" (L) L8'
L7 12 "TWO MUTATIONS" (L) L3

> L1 and L2
L8 106 L1 AND L2

=> S2 and L8
L9 5 S2 AND L8

=> mutation and L8
L10 100 MUTATION AND L8

=> "stop codones" and L10
L11 0 "STOP CODONES" AND L10

=> deletion and L10
L12 29 DELETION AND L10

=> D L9 IBIB ABS 1-5

=>
=> EIAV and S2
L13 37 EIAV AND S2

=> D L13 IBIB T 1-37
'T' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):TI

L13 ANSWER 1 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Genomic sequence anal. of proviral Chinese donkey leukocyte attenuated equine infectious anemia virus vaccine strain

L13 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI A live attenuated equine infectious anemia virus proviral vaccine with a modified **S2** gene provides protection from detectable infection by intravenous virulent virus challenge of experimentally inoculated horses

L13 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Characterization of a cytolytic strain of equine infectious anemia virus

L13 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Proviral genomic sequence analysis of Chinese donkey leukocyte attenuated equine infectious anemia virus vaccine and its parental virus strain Liaoning

L13 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Equine infectious anemia challenge model for testing vaccines, diagnostics, and treatments

L13 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Equine infectious anemia vaccine

L13 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Complete sequence of proviral DNA of Equine infectious anemia virus L strain

L13 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Full-length sequences of Equine infection anemia virus (**EIAV**) LN and its attenuated strain FD and their in diagnosis and vaccine development

L13 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Equine infectious anemia virus proteins with epitopes most frequently recognized by cytotoxic T lymphocytes from infected horses

L13 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI The full-length equine infectious anemia virus (**EIAV**) genomic sequence of a donkey leukocyte vaccine strain

L13 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Characterization of the equine infectious anaemia virus **S2** protein

L13 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Mutations occurring during serial passage of Japanese equine infectious anemia virus in primary horse macrophages

L13 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI The **S2** gene of equine infectious anemia virus is a highly

conserved determinant of viral replication and virulence properties in experimentally infected ponies

L13 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Equine infectious anemia virus-based retroviral vectors

L13 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI The **S2** gene of equine infectious anemia virus is dispensable for viral replication in vitro

L13 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Development and characterization of an in vivo pathogenic molecular clone of equine infectious anemia virus

L13 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Helix-stabilizing agent, CC-1065, enhances suppression of translation by an antisense oligodeoxynucleotide

L13 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI The surface envelope protein gene region of equine infectious anemia virus is not an important determinant of tropism in vitro

L13 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Analysis of multiple mRNAs from pathogenic equine infectious anemia virus (**EIAV**) in an acutely infected horse reveals a novel protein, Ttm, derived from the carboxy terminus of the **EIAV** transmembrane protein

L13 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Molecular model of equine infectious anemia virus proteinase and kinetic measurements for peptide substrates with single amino acid substitutions

L13 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Equine infectious anemia virus gene expression: characterization of the RNA splicing pattern and the protein products encoded by open reading frames S1 and **S2**

L13 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Identification of sequences encoding the equine infectious anemia virus tat gene

L13 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI Pattern of transcription of the genome of equine infectious anemia virus

L13 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
TI **EIAV** genomic organization: further characterization by sequencing of purified glycoproteins and cDNA

L13 ANSWER 25 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI A live attenuated equine infectious anemia virus proviral vaccine with a modified **S2** gene provides protection from detectable infection by intravenous virulent virus challenge of experimentally inoculated horses.

L13 ANSWER 26 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Characterization of a cytolytic strain of equine infectious anemia virus.

L13 ANSWER 27 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Proviral genomic sequence analysis of Chinese donkey leukocyte attenuated equine infectious anemia virus vaccine and its parental virus strain Liaoning.

L13 ANSWER 28 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Equine infectious anaemia virus proteins with epitopes most frequently recognized by cytotoxic T lymphocytes from infected horses.

L13 ANSWER 29 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Characterization of the equine infectious anaemia virus **S2** protein.

L13 ANSWER 30 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Mutations occurring during serial passage of Japanese equine infectious anemia virus in primary horse macrophages.

L13 ANSWER 31 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI The **S2** gene of equine infectious anemia virus is a highly conserved determinant of viral replication and virulence properties in experimentally infected ponies.

L13 ANSWER 32 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI The **S2** gene of equine infectious anemia virus is dispensable for viral replication in vitro.

L13 ANSWER 33 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Development and characterization of an in vivo pathogenic molecular clone of equine infectious anemia virus.

L13 ANSWER 34 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Molecular model of equine infectious anemia virus proteinase and kinetic measurements for peptide substrates with single amino acid substitutions.

L13 ANSWER 35 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Analysis of multiple mRNAs from pathogenic equine infectious anemia virus (**EIAV**) in an acutely infected horse reveals a novel protein, Ttm, derived from the carboxyl terminus of the **EIAV** transmembrane protein.

L13 ANSWER 36 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI EQUINE INFECTIOUS ANEMIA VIRUS GENE EXPRESSION CHARACTERIZATION OF THE RNA SPLICING PATTERN AND THE PROTEIN PRODUCTS ENCODED BY OPEN READING FRAMES S1 AND **S2**.

L13 ANSWER 37 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI IDENTIFICATION OF SEQUENCES ENCODING THE EQUINE INFECTIOUS ANEMIA VIRUS TAT GENE.

=> D L13 IBIB ABS 1 2 5 6 11 25

L13 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:665082 CAPLUS
DOCUMENT NUMBER: 134:96760
TITLE: Characterization of the equine infectious anaemia virus **S2** protein
AUTHOR(S): Yoon, Soonsang; Kingsman, Susan M.; Kingsman, Alan J.; Wilson, Stuart A.; Mitrophanous, Kyriacos A.
CORPORATE SOURCE: Retrovirus Molecular Biology Group, Department of Biochemistry, University of Oxford, Oxford, OX1 3QU, UK
SOURCE: Journal of General Virology (2000), 81(9), 2189-2194
CODEN: JGVIAY; ISSN: 0022-1317
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **S2** is an accessory protein of equine infectious anemia virus (**EIAV**), the function of which is unknown. In order to gain insight into the function of **S2**, the intracellular localization of the protein, its interaction with viral proteins and its incorporation into viral particles have been investigated. Immunolocalization of **S2** revealed punctate staining in the cytoplasm and the **S2** protein copptd. with the **EIAV** Gag precursor. Despite overexpression of **S2** through the use of a codon-optimized sequence, there was no preferential association of **S2** with **EIAV** particles. These data suggest that **S2** may function to organize the Gag protein during particle assembly in the cytoplasm but that it is unlikely to be involved in the early stages of the virus life-cycle.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 25 OF 37 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:345091 BIOSIS
DOCUMENT NUMBER: PREV200300345091
TITLE: A live attenuated equine infectious anemia virus proviral vaccine with a modified **S2** gene provides protection from detectable infection by intravenous virulent virus challenge of experimentally inoculated horses.
AUTHOR(S): Li, Feng; Craigo, Jodi K.; Howe, Laryssa; Steckbeck, Jonathan D.; Cook, Sheila; Issel, Charles; Montelaro, Ronald C. [Reprint Author]
CORPORATE SOURCE: Department of Molecular Genetics and Biochemistry, University of Pittsburgh School of Medicine, W1144 Biomedical Science Tower, Pittsburgh, PA, 15261, USA
rmont@pitt.edu
SOURCE: Journal of Virology, (July 2003) Vol. 77, No. 13, pp. 7244-7253. print.
ISSN: 0022-538X (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003
AB Previous evaluations of inactivated whole-virus and envelope subunit vaccines to equine infectious anemia virus (**EIAV**) have revealed a broad spectrum of efficacy ranging from highly type-specific protection to severe enhancement of viral replication and disease in experimentally immunized equids. Among experimental animal lentivirus vaccines, immunizations with live attenuated viral strains have proven most effective, but the vaccine efficacy has been shown to be highly dependent on the nature and severity of the vaccine virus attenuation. We describe here for the first time the characterization of an experimental attenuated proviral vaccine, EIAVUKDELTAS2, based on inactivation of the **S2** accessory gene to down regulate in vivo replication without affecting in

vitro growth properties. The results of these studies demonstrated that immunization with EIAVUKDELTAS2 elicited mature virus-specific immune responses by 6 months and that this vaccine immunity provided protection from disease and detectable infection by intravenous challenge with a reference virulent biological clone, EIAVPV. This level of protection was observed in each of the six experimental horses challenged with the reference virulent EIAVPV by using a low-dose multiple-exposure protocol (three administrations of 10 median horse infectious doses (HID50), intravenous) designed to mimic field exposures and in all three experimentally immunized ponies challenged intravenously with a single inoculation of 3,000 HID50. In contrast, naive equids subjected to the low- or high-dose challenge develop a detectable infection of challenge virus and acute disease within several weeks. Thus, these data demonstrate that the **EIAV S2** gene provides an optimal site for modification to achieve the necessary balance between attenuation to suppress virulence and replication potential to sufficiently drive host immune responses to produce vaccine immunity to viral exposure.

L12 ANSWER 21 OF 29 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1998:41355 BIOSIS
DN PREV199800041355
TI Novel and dynamic evolution of **equine infectious anemia virus** genomic quasispecies associated with sequential disease cycles in an experimentally infected pony.
AU Leroux, Caroline; Issel, Charles J.; Montelaro, Ronald C. [Reprint author]
CS Dep. Molecular Genetics Biochemistry, Univ. Pittsburgh Sch. Med., Pittsburgh, PA 15261, USA
SO Journal of Virology, (Dec., 1997) Vol. 71, No. 12, pp. 9627-9639. print. CODEN: JOVIAM. ISSN: 0022-538X.
DT Article
LA English
OS Genbank-AF05104; Genbank-AF05105; Genbank-AF05106; Genbank-AF05107; Genbank-AF05108; Genbank-AF05109; Genbank-AF05110; Genbank-AF05111; Genbank-AF05112; Genbank-AF05113; Genbank-AF05114; Genbank-AF05115; Genbank-AF05116; Genbank-AF05117; Genbank-AF05118; Genbank-AF05119; Genbank-AF05120; Genbank-AF05121; Genbank-AF05122; Genbank-AF05123; Genbank-AF05124; Genbank-AF05125; Genbank-AF05126; Genbank-AF05127; Genbank-AF05128; Genbank-AF05129; Genbank-AF05130; Genbank-AF05131; Genbank-AF05132; Genbank-AF05133; Genbank-AF05134; Genbank-AF05135; Genbank-AF05136; Genbank-AF05137; Genbank-AF05138; Genbank-AF05139; Genbank-AF05140; Genbank-AF05141; Genbank-AF05142; Genbank-AF05143; Genbank-AF05144; Genbank-AF05145; Genbank-AF05146; Genbank-AF05147; Genbank-AF05148; Genbank-AF05149; Genbank-AF05150; Genbank-AF05151
ED Entered STN: 14 Jan 1998
Last Updated on STN: 14 Jan 1998
AB We have investigated the genetic evolution of three functionally distinct regions of the **equine infectious anemia virus** (**EIAV**) genome (env, rev, and long terminal repeat) during recurring febrile episodes in a pony experimentally infected with a well-characterized reference biological clone designated EIAVPV. Viral populations present in the plasma of an EIAVPV-infected pony during sequential febrile episodes (18, 34, 80, 106, and 337 days postinfection) were amplified from viral RNA, analyzed, and compared to the inoculated strain. The comparison of the viral quasispecies showed that the inoculated EIAVPV quasispecies were all represented during the first febrile episode, but entirely replaced at the time of the second febrile episode, and that new predominant quasispecies were associated with each subsequent cycle of disease. One of the more surprising results was the in vivo generation of large **deletion** (up to 15 amino acids) in the principal neutralizing domain (PND) of gp90 during the third febrile episode. This **deletion** did not alter the competence for in vitro replication as shown by the analysis of a env chimeric clone with a partially deleted PND and did not altered the fitness of the virus in vivo, since this partially deleted envelope became the major population during the fourth febrile episode. Finally, we showed that the amino acid **mutations** were not randomly distributed but delineated eight variables regions, V1 to V8, with V3 containing the PND region. These studies provide the first detailed description of the evolution of **EIAV** genomic quasispecies during persistent infection and reveal new insights into the genetics and potential mechanisms of lentivirus genomic variation.

L12 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:289434 CAPLUS
DN 126:340303
TI Characterization and mutational studies of **equine infectious anemia virus** dUTPase
AU Shao, Hai; Robek, Michael D.; Threadgill, Deborah S.; Mankowski, Lori S.; Cameron, Craig E.; Fuller, Frederick J.; Payne, Susan L.
CS Department of Molecular Biology and Microbiology, Case Western Reserve University School of Medicine, 10900 Euclid Avenue, Cleveland, OH, USA
SO Biochimica et Biophysica Acta (1997), 1339(2), 181-191
CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier
DT Journal
LA English
AB The macrophage tropic lentivirus, **equine infectious anemia virus** (**EIAV**), encodes a dUTPase in the pol gene that is required for efficient replication in macrophages. Two naturally occurring variants of the enzyme were expressed as recombinant proteins in Escherichia coli; metal chelate affinity chromatog. was used to purify histidine-tagged recombinant enzymes to greater than 80% homogeneity in a single chromatog. step. Biochem. and enzymic analyses of these prepns. suggest that this method yields dUTPase that is suitable for detailed mutational anal. Specific activities of prepns. ranged from 4+103 to 5+104 units/mg. Recombinant **EIAV** dUTPase was highly specific for dUTP with a Km in the range of 3 to 8 μM. The enzyme was sensitive to inhibition by dUDP with little inhibition by other nucleotides or the reaction products, dUMP and PPi. The subunit organization of recombinant **EIAV** dUTPase was probed by gel filtration, glycerol gradient centrifugation, and chemical crosslinking, and is a trimer. We have begun mutational analyses by targeting a conserved domain present at the carboxyl terminus of all dUTPases that shares high homol. to the phosphate binding loops (P-loops) of a number of ATP- and GTP-binding phosphatases. The P-loop-like motif of dUTPases is glycine rich but lacks the invariant lysine found in authentic P-loops. **Deletion** of this motif leads to loss of dUTPase activity; a series of point **mutations** that have been shown to inactivate authentic P-loops also abolish **EIAV** dUTPase activit

L12 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:745048 CAPLUS
DN 128:72864
TI Novel and dynamic evolution of **equine infectious anemia virus** genomic quasispecies associated with sequential disease cycles in an experimentally infected pony
AU Leroux, Caroline; Issel, Charles J.; Montelaro, Ronald C.
CS Dep. of Mol. Genet. and Biochem., Univ. of Pittsburgh Sch. of Med., Pittsburgh, PA, 15261, USA
SO Journal of Virology (1997), 71(12), 9627-9639
CODEN: JOVIAM; ISSN: 0022-538X
PB American Society for Microbiology
DT Journal
LA English
AB We have investigated the genetic evolution of three functionally distinct regions of the **equine infectious anemia virus** (**EIAV**) genome (env, rev, and long terminal repeat) during recurring febrile episodes in a pony exptl. infected with a well-characterized reference biol. clone designated EIAVPV. Viral populations present in the plasma of an EIAVPV-infected pony during sequential febrile episodes (17, 34, 80, 106, and 337 days postinfection) were amplified from viral RNA, analyzed, and compared to the inoculated strain. The comparison of the viral quasispecies showed that the inoculated EIAVPV quasispecies were all represented during the first febrile episode, but entirely replaced at the time of the second febrile episode, and that new predominant quasispecies were associated with each subsequent cycle of disease. One of the more surprising results was the in vivo generation of large **deletion** (up to 15 amino acids) in the principal neutralizing domain (PND) of gp90 during the third febrile episode. This **deletion** did not alter the competence for in vitro replication as shown by the anal. of a env chimeric clone with a partially deleted PND and did not alter the fitness of the virus in vivo, since this partially deleted envelope became the major population during the fourth febrile episode. Finally, we showed that the amino acid **mutations** were not randomly distributed but delineated eight variables regions, V1 to V8, with V3 containing the PND region. These studies provide the first detailed description of the evolution of **EIAV** genomic quasispecies during persistent infection and reveal new insights into the genetics and potential mechanisms of lentivirus genomic variation

L12 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:62176 CAPLUS
DN 128:176801
TI Genetic variation of envelope gp90 gene of **equine infectious anemia virus** isolated from an experimentally infected horse
AU Pang, Hai; Kong, Xian-Gang; Sentsui, Hiroshi; Kono, Yuji; Sugiura, Takeo; Hasegawa, Atsuhiko; Akashi, Hiroomi
CS National Inst. Animal Health, Ibaraki, Japan
SO Journal of Veterinary Medical Science (1997), 59(12), 1089-1095
CODEN: JVMSEQ; ISSN: 0916-7250
PB Japanese Society of Veterinary Science
DT Journal
LA English
AB Six strains of **equine infectious anemia virus** (**EIAV**) were recovered from febrile and non-febrile stages of a horse exptl. infected with the P337-V70 strain given once to a horse. The env gp90 genes of the isolates, the P337-V70 and P337-V26, avirulent virus derived from the P337-V70 strain, were sequenced. A comparison of the gp90 gene sequences revealed that amino acid variations among the viruses tested showed as high as 8.2 to 11.5%. In addition, the comparison also indicated that isolates recovered from the non-febrile stage contained nucleotide insertions in the principal neutralizing domain (PND) region. The insertions were arranged regularly with smaller segments. The nucleotide sequence of the P337-V26 gp90 gene was found to contain a six-nucleotides insertion and seven nucleotide substitutions outside the PND region, when compared with that of the P337-V70 strain

L9 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2000:408620 BIOSIS
DOCUMENT NUMBER: PREV200000408620
TITLE: **Mutations** occurring during serial passage of Japanese **equine infectious anemia virus** in primary horse macrophages.
AUTHOR(S): Zheng, Yong-Hui; Sentsui, Hiroshi; Kono, Yuji; Ikuta, Kazuyoshi [Reprint author]
CORPORATE SOURCE: Institute of Immunological Science, Hokkaido University, Kita-ku, Sapporo, Japan
SOURCE: Virus Research, (June, 2000) Vol. 68, No. 1, pp. 93-98. print.
CODEN: VIREDF. ISSN: 0168-1702.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Sep 2000
Last Updated on STN: 8 Jan 2002

AB An attenuated **equine infectious anemia Virus** (**EIAV**), named V26, was previously obtained after 50 passages of the Japanese virulent strain V70 in primary macrophage culture. To clarify the differences between both viruses, their full-length sequences were determined. There were higher **mutations** in **S2** (6.15% amino acid difference) and LTR (10.7% nucleotide difference). The presumed initiation codon of the **S2** gene was absent from the sequence of V26. There was a large insertion within the long-terminal repeat (LTR) U3 hypervariable region of V26. In addition, there were minor **mutations** in gag (1.22% amino acid difference), pol (1.05% amino acid difference) and env (1.65% amino acid difference) regions, but no **mutation** in tat region. No **mutations** were observed in the principal neutralizing domain in the gp90. Thus, the **mutations** in the **S2** and LTR might be the major target sites of **mutation** in

L9 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:564346 BIOSIS
DOCUMENT NUMBER: PREV200200564346
TITLE: Proviral genomic sequence analysis of Chinese donkey leukocyte attenuated **equine infectious anemia virus** vaccine and its parental virus strain Liaoning.
AUTHOR(S): Wang Liu; Tong Guangzhi [Reprint author]; Liu Hongquan; Yang Zhibiao; Qiu Huaji; Kong Xiangang; Wang Mei
CORPORATE SOURCE: National Key Laboratory of Veterinary Biotechnology, Harbin Veterinary Research Institute, Chinese Academy of Agricultural Sciences, Harbin, 150001, China
gztong@public.hr.hl.cn
SOURCE: Science in China Series C Life Sciences, (February, 2002) Vol. 45, No. 1, pp. 57-67. print.
ISSN: 1006-9305.
DOCUMENT TYPE: Article
LANGUAGE: English
OTHER SOURCE: Genbank-AF028231; EMBL-AF028231; DDBJ-AF028231; Genbank-AF028232; EMBL-AF028232; DDBJ-AF028232; Genbank-AF332738; EMBL-AF332738; DDBJ-AF332738; Genbank-AF332741; EMBL-AF332741; DDBJ-AF332741; Genbank-M16575; EMBL-M16575; DDBJ-M16575; Genbank-M87581; EMBL-M87581; DDBJ-M87581; Genbank-U10866; EMBL-U10866; DDBJ-U10866
ENTRY DATE: Entered STN: 30 Oct 2002
Last Updated on STN: 30 Dec 2002

AB Proviral DNA was extracted from donkey leukocyte infected with Chinese donkey leukocyte attenuated **equine infectious anemia virus** (DLA-**EIAV**), and peripheral blood lymphocytes (PBL) from a horse infected with the virulent **EIAV** strain Liaoning (**EIAV** L). The entire proviral DNA from both viruses was cloned and sequenced. The lengths of complete genomic sequences of DLA-**EIAV** and **EIAV** L provirus were 8266 bp and 8235 bp, respectively. Sequence comparison indicated that DLA-**EIAV** shares 97.0% and 97.5% in sequence homology with **EIAV** L and donkey-adapted **EIAV** (DA-**EIAV**), respectively. Lots of variations occurred in long terminal repeat (LTR, consisting of U3, R, U5), ORF **S2**, and env regions between DLA-**EIAV** and **EIAV** L. The nucleotide sequence differences of the two viruses in U3, R, U5, ORF **S2**, and env are 13.2%, 7.5%, 5.1%, 3.9%, and 2.7%, respectively, and predicted amino acid sequence differences in env and **S2** coding regions are 4.4% and 8.8%, respectively. Six conserved regions are characterized in Gp90. There is a cis-activating GATA motif in ENH of DLA-**EIAV** and **EIAV** L. Two N-linked glycosylation sites disappeared in DLA-**EIAV** Gp90 in comparison with that of **EIAV** L. A. bHLH transcription factor binding consensus sequence was found in LTR of DLA-**EIAV** but not in **EIAV** L. Furthermore, there is a **mutation** in the stem of DLA-**EIAV** TAR resulting in formation of a uridine tuber. Further study is needed to uncover the relationship between sequence changes and their biological functions of DLA-**EIAV** and L.

L13 ANSWER 1 OF 37 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:646931 CAPLUS
DOCUMENT NUMBER: 139:144997
TITLE: Genomic sequence anal. of proviral Chinese donkey leukocyte attenuated equine infectious anemia virus vaccine strain
INVENTOR(S): Dong, Guangzhi; Wang, Liu; Yang, Zhibiao; Liu, Hongquan; Qiu, Huaji; Kong, Xiangang
PATENT ASSIGNEE(S): Harbin Inst. of Veterinary Medicine, Chinese Academy of Agricultural Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 18 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1366053	A	20020828	CN 2001-101487	20010118

PRIORITY APPLN. INFO.: CN 2001-101487 20010118

AB Disclosed is the genomic sequence of proviral Chinese donkey leukocyte attenuated equine infectious anemia virus vaccine strain (DLA-**EIAV**) comprising full-length long terminal repeat (LTR) of 5'-end of **EIAV** DLA pro-virus, structural genes (gag, pol, env), small open-reading frames (S1, **S2**, S3), and full-length LTR of 3'-end. The reverse transcriptase activity and infectivity of DLA-**EIAV** is demonstrated.

```
=> formalin (l) DNA
         21049 FORMALIN
             2 FORMALINS
         21050 FORMALIN
                 (FORMALIN OR FORMALINS)
        685419 DNA
         17360 DNAS
        688096 DNA
                 (DNA OR DNAS)
L1        1175 FORMALIN (L) DNA

=> vaccine and L1
         45403 VACCINE
         46217 VACCINES
         57074 VACCINE
                 (VACCINE OR VACCINES)
L2          34 VACCINE AND L1

=> "DNA vaccine"
        685419 "DNA"
         17360 "DNAS"
        688096 "DNA"
                 ("DNA" OR "DNAS")
         45403 "VACCINE"
         46217 "VACCINES"
         57074 "VACCINE"
                 ("VACCINE" OR "VACCINES")
L3        3155 "DNA VACCINE"
                 ("DNA"(W)"VACCINE")

=> formalin and L3
         21049 FORMALIN
             2 FORMALINS
         21050 FORMALIN
                 (FORMALIN OR FORMALINS)
L4          17 FORMALIN AND L3

=> D L4 IBIB ABS 1-17

L4   ANSWER 1 OF 17  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        2004:582083  CAPLUS
TITLE:                   West Nile virus vaccines
AUTHOR(S):               Hall, Roy A.; Khromykh, Alexander A.
CORPORATE SOURCE:        Department of Microbiology and Parasitology, The
                         University of Queensland, Queensland, 4072, Australia
SOURCE:                  Expert Opinion on Biological Therapy (2004), 4(8),
                         1295-1305
                         CODEN: EOBTA2; ISSN: 1471-2598
PUBLISHER:               Ashley Publications Ltd.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   West Nile virus (WNV) is a mosquito-borne flavivirus that is emerging as a
     global pathogen.  In the last decade, virulent strains of the virus have
     been associated with significant outbreaks of human and animal disease in
     Europe, the Middle East and North America.  Efforts to develop human and
     veterinary vaccines have taken both traditional and novel approaches.  A
     formalin-inactivated whole virus vaccine has been approved for use
     in horses.  DNA vaccines coding for the structural WNV
     proteins have also been assessed for veterinary use and have been found to
     be protective in mice, horses and birds.  Live attenuated yellow fever WNV
     chimeric vaccines have also been successful in animals and are currently
     undergoing human trials.  Addnl. studies have shown that immunization with
     a relatively benign Australian variant of WNV, the Kunjin virus, also
     provides protective immunity against the virulent North American strain.
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Levels of efficacy and safety, as well as logistical, economic and environmental issues, must all be carefully considered before vaccine candidates are approved and selected for large-scale manufacture and distribution.

REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:126339 CAPLUS
DOCUMENT NUMBER: 140:285838
TITLE: A protective effect of epidermal powder immunization in a mouse model of equine herpesvirus-1 infection
AUTHOR(S): Kondo, Takashi; McGregor, Martha; Chu, Qili; Chen, Dexiang; Horimoto, Taisuke; Kawaoka, Yoshihiro
CORPORATE SOURCE: Japan Racing Association, Epizootic Research Station, Equine Research Institute, Tochigi, 329-0412, Japan
SOURCE: Virology (2004), 318(1), 414-419
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To evaluate the protective effect of epidermal powder immunization (EPI) against equine herpesvirus-1 (EHV-1) infection, the authors prepared a powder vaccine in which **formalin**-inactivated virions were embedded in water-soluble, sugar-based particles. A PowderJect device was used to immunize mice with the powder vaccine via their abdominal skin. The authors found that twice-immunized mice were protected against challenge with the wild-type virus. This protective effect was equivalent to or better than that observed in mice immunized with other types of vaccines, including a gene gun-mediated **DNA vaccine** containing the glycoprotein D (gD) gene or conventional inactivated virus vaccines introduced via i.m. or intranasal injections. These findings indicate that the powder vaccine is a promising approach for the immunol. control of EHV-1 infection, either alone or as a part of prime-boost vaccination strategies.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:681408 CAPLUS
DOCUMENT NUMBER: 139:306132
TITLE: A role for nonprotective complement-fixing antibodies with low avidity for measles virus in atypical measles
AUTHOR(S): Polack, Fernando P.; Hoffman, Scott J.; Crujeiras, Gonzalo; Griffin, Diane E.
CORPORATE SOURCE: W. Harry Feinstone Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, 21205, USA
SOURCE: Nature Medicine (New York, NY, United States) (2003), 9(9), 1209-1213
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the 1960s, a **formalin**-inactivated measles vaccine (FIMV) predisposed recipients to atypical measles, an immune complex-mediated disease. To identify characteristics of the immune priming that leads to atypical measles, responses of monkeys to FIMV were compared with responses to live attenuated virus (LAV) and hemagglutinin (H-**DNA**) **vaccines** that do not prime for atypical measles. Antibodies induced by FIMV were transient and avidity did not mature. Antibodies induced by LAV and H-**DNA vaccines** were sustained and avidity matured over time. After challenge with measles virus, FIMV and H-DNA recipients developed high titers of complement-fixing antibodies.

In FIMV recipients, the antibodies were of low avidity, whereas in H-**DNA vaccine** recipients, the antibodies were of high avidity. Neutralizing capacity in B958 cells correlated with avidity. Only FIMV recipients had immune complex deposition. Failure of FIMV to induce affinity maturation results in anamnestic production of nonprotective, complement-fixing antibodies, immune complex deposition, and atypical measles.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:414974 CAPLUS
DOCUMENT NUMBER: 139:212399
TITLE: Traditional and novel approaches to flavivirus vaccines
AUTHOR(S): Pugachev, Konstantin V.; Guirakhoo, Farshad; Trent, Dennis W.; Monath, Thomas P.
CORPORATE SOURCE: Acambis, Inc., Cambridge, MA, 02139, USA
SOURCE: International Journal for Parasitology (2003), 33(5-6), 567-582
CODEN: IJPYBT; ISSN: 0020-7519
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Yellow fever, dengue, Japanese encephalitis and tick-borne encephalitis viruses are the medically most important members of the Flavivirus genus composed primarily of arboviruses. In this paper, we review the com. available traditional flavivirus vaccines against yellow fever, Japanese encephalitis, and tick-borne encephalitis, as well as modern approaches to flavivirus vaccines. **Formalin** inactivation technol. has been employed to produce killed vaccines. Flaviviruses have been attenuated by multiple passages in animal tissues and cell cultures to produce empirical live attenuated vaccines. The use of traditional methods is being pursued to develop vaccines against other flavivirus diseases, such as dengue, and to improve existing vaccines, such as for Japanese encephalitis. With the recent development of infectious clones, rational approaches to attenuated flavivirus vaccines have employed the introduction of specific mutations into wild type viruses and chimerization between different viruses. Novel methods for delivery of live vaccines, such as inoculation of infectious DNA or RNA, have been described. Other approaches, such as the construction of protein subunit, expression vector-based and naked **DNA vaccines**, have been proposed to create alternate vaccine candidates.

REFERENCE COUNT: 133 THERE ARE 133 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:256061 CAPLUS
DOCUMENT NUMBER: 136:261820
TITLE: Swine vaccines for proliferative ileitis comprising Lawsonia intracellularis antigens
PATENT ASSIGNEE(S): University of Arizona, Board of Regents, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002026250	A2	20020404	WO 2001-US30284	20010927
WO 2002026250	A3	20030501		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001093151	A5	20020408	AU 2001-93151		20010927
EP 1324768	A2	20030709	EP 2001-973589		20010927
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004529854	T2	20040930	JP 2002-530080		20010927
PRIORITY APPLN. INFO.:			US 2000-677108	A	20000929
			WO 2001-US30284	W	20010927

AB A proliferative ileitis vaccine comprising tissue culture grown Lawsonia intracellularis and methods of making said vaccines. Proliferative ileitis vaccines described include those containing whole L. intracellularis, exts. of L. intracellularis, protective immunogenic submits of L. intracellularis, recombinant immunogens of L. intracellularis and naked DNA of L. intracellularis. The vaccines of this invention may be inactivated or modified live and contain adjuvants and/or stabilizers. The vaccines of this invention may be in a liquid or lyophilized form. Also disclosed are monoclonal antibodies which neutralize the growth of L. intracellularis and which may be used for diagnosing proliferative ileitis as well as for quantitating antigen during vaccine production

L4 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2002:75162 CAPLUS
DOCUMENT NUMBER:	137:45548
TITLE:	Prospects for development of a vaccine against the West Nile virus
AUTHOR(S):	Monath, Thomas P.
CORPORATE SOURCE:	Research and Medical Affairs, Acambis Incorporated, Cambridge, MA, 02139, USA
SOURCE:	Annals of the New York Academy of Sciences (2001), 951(West Nile Virus), 1-12 CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER:	New York Academy of Sciences
DOCUMENT TYPE:	Journal; General Review
LANGUAGE:	English

AB A review. Vaccination provides the ultimate measure for personal protection against West Nile disease. A review. The development of a West Nile vaccine for humans is justified by the uncertainty surrounding the size and frequency of future epidemics. At least two companies (Acambis Inc. and Baxter/Immuno) have initiated research and development on human vaccines. West Nile encephalitis has also emerged as a significant problem for the equine industry. One major veterinary vaccine manufacturer (Ft. Dodge) is developing **formalin**-inactivated and naked **DNA vaccines**. The advantages and disadvantages of **formalin**-inactivated whole virion vaccines, Japanese encephalitis vaccine for cross-protection, naked DNA, and live attenuated vaccines are described. A novel technol. platform for live, attenuated recombinant vaccines (ChimeriVax) represents a promising approach for rapid development of a West Nile vaccine. This technol. uses yellow fever 17D as a live vector for envelope genes of the West Nile virus. Infectious clone technol. is used to replace the genes encoding the prM and E structural proteins of yellow fever 17D vaccine virus with the corresponding genes of West Nile virus. The resulting virion has the protein coat of West Nile, containing all antigenic determinants for neutralization and one or more epitopes for cytotoxic T lymphocytes. The genes encoding the nucleocapsid protein, nonstructural proteins, and untranslated terminal regions responsible for replication remain those of

the original yellow fever 17D virus. The chimeric virus replicates in the host like yellow fever 17D but immunizes specifically against West Nile virus.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:786754 CAPLUS
DOCUMENT NUMBER: 135:343278
TITLE: Japanese encephalitis **DNA vaccines** expressing premembrane and envelope genes for swine immunization
INVENTOR(S): Mason, Peter W.; Konishi, Eiji; Yamaoka, Masaoki; Kurane, Ichiro
PATENT ASSIGNEE(S): National Institute Infectious Diseases, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 28 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001299355	A2	20011030	JP 2000-126989	20000427
PRIORITY APPLN. INFO.:			JP 2000-126989	20000427

AB Japanese encephalitis **DNA vaccines** expressing premembrane (prM) and envelope genes (E) and use in immunization of mammals, are disclosed. The recombinant plasmid vector contains prM signal peptide, prM gene, E gene, promoter, cytomegalovirus derived intron A, non-SV40 derived origin of replication, kanamycin resistance gene, and immuno stimulatory sequence, ie. ampicillin resistance gene (amp). Swine are an important amplifier of Japanese encephalitis (JE) virus in the paradomestic environment. In this study, two JE **DNA vaccine** candidates were evaluated for immunogenicity in swine. Both vaccine plasmids encode a cassette consisting of the signal of premembrane (prM), prM, and envelope (E) coding regions of JE virus. One plasmid, designated pcJEME, is based on a com. vector (pcDNA3), whereas the other plasmid, designated pNJEME, is based on a vector (pNGVL4a) designed to address some of the safety concerns of **DNA vaccine** use. No differences were detected in the immunogenicity of these two plasmids in mice or swine. Swine immunized with the **DNA vaccines** at a dose of 100 to 450 μg at an interval of 3 wk developed neutralizing and hemagglutination-inhibitory (HAI) antibody titers of 1:40 to 1:160 at 1 wk after the second immunization. However, swine administered two doses of a com. JE vaccine (**formalin**-inactivated virus preparation; JEVAX-A) developed low (1:10) or undetectable antibody responses after their boost. Interestingly, serum antibody titers elicited by **DNA vaccines** in swine were higher than those detected in mice. Eight days after boosting with viral antigen (JEVAX-A) to detect an anamnestic response, swine immunized two times with the **DNA vaccine** showed a >100-fold elevation in HAI titer, indicating a strong recall of antibody response. Swine maintained detectable levels of HAI antibody for at least 245 days after two immunizations with a **DNA vaccine**. These results indicate that these **DNA vaccines** are able to induce virus-specific memory B cells and long-lasting antibodies in swine, which were of higher levels than those obtained with a com. **formalin**-inactivated JE vaccine.

L4 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:609462 CAPLUS
DOCUMENT NUMBER: 136:277556
TITLE: Host responses against the fish parasitizing ciliate

Ichthyophthirius multifiliis
AUTHOR(S): Buchmann, K.; Sigh, J.; Nielsen, C. V.; Dalgaard, M.
CORPORATE SOURCE: Section of Fish Diseases, Department of Veterinary Microbiology, Royal Veterinary and Agricultural University, Frederiksberg, DK-1870, Den.
SOURCE: Veterinary Parasitology (2001), 100(1-2), 105-116
CODEN: VPARDI; ISSN: 0304-4017
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Recent studies have shown that fish are able to mount protective immune responses against various parasites. One of the best characterized parasite-host system in this context is the ciliate Ichthyophthirius multifiliis (Ich) parasitizing a range of freshwater fishes. Both specific and non-specific host defense mechanisms are responsible for the protection of fish against challenge infections with this ciliate. The specific humoral components comprise at least specific antibodies. The non-specific humoral elements included are the alternative complement pathway and probably lectins. Cellular factors involved in the specific response are B-cells and putative T-cells. The non-specific effector cells recognized are various leukocytes. In addition, goblet-cells and mast cells (EGC-cells) may have a function. The NCC-cell (suggested analog to NK-cells in mammals) seems to play a role in the non-specific response. This well documented protective response in freshwater fishes against Ich has urged the development of anti-parasitic vaccines. Indeed, such products based on **formalin** killed parasites have been developed and found to offer the vaccinated host a satisfactory protection. However, the collection of parasites for vaccine production is extremely laborious. It involves keeping infected fish due to the fact that in vitro propagation of the parasite is still insufficiently developed. Gaining knowledge of amino acid sequences and its encoding DNA-sequences for the protective antigens (i-antigens) in the parasite was a major breakthrough. That achievement made it possible to produce a recombinant protein in E. coli and preliminary results indicated a certain protection of fish vaccinated with this product. Recent work has shown that the free-living and easily cultivated ciliate Tetrahymena can be transformed and express the i-antigen. This path seems to be promising for future development of vaccines against Ich. A novel approach in fish is the development of **DNA-vaccines**. Successful DNA-vaccination trials have been conducted in fish against viral infections and the technol. also makes it possible to develop a **DNA-vaccine** against Ich. Other approaches to immuno-protection against Ich have been the use of heterologous vaccines. Thus, both bath and injection vaccination using live or killed (un-transformed) Tetrahymena has been reported to offer treated fish a certain level of protection. Such protection could be explained by non-specific reactions and the efficacy and duration of this vaccination type should be further evaluated.
REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:502638 CAPLUS
DOCUMENT NUMBER: 133:191698
TITLE: Successful DNA immunization against measles: Neutralizing antibody against either the hemagglutinin or fusion glycoprotein protects rhesus macaques without evidence of atypical measles
AUTHOR(S): Polack, Fernando P.; Lee, Sok H.; Permar, Sallie; Manyara, Elizabeth; Nousari, Hossein G.; Jeng, Yaikah; Mustafa, Farah; Valsamakis, Alexandra; Adams, Robert J.; Robinson, Harriet L.; Griffin, Diane E.
CORPORATE SOURCE: W. Harry Feinstone Department of Molecular Microbiology and Immunology, Johns Hopkins University

School of Hygiene and Public Health, Baltimore, MD, 21205, USA
SOURCE: Nature Medicine (New York) (2000), 6(7), 776-781
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Measles remains a principal cause of worldwide mortality, in part because young infants cannot be immunized effectively. Development of new vaccines has been hindered by previous experience with a **formalin**-inactivated vaccine that predisposed to a severe form of disease (atypical measles). Here we have developed and tested potential **DNA vaccines** for immunogenicity, efficacy and safety in a rhesus macaque model of measles. DNA protected from challenge with wild-type measles virus. Protection correlated with levels of neutralizing antibody and not with cytotoxic T lymphocyte activity. There was no evidence in any group, including those receiving hemagglutinin-encoding DNA alone, of 'priming' for atypical measles.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:120388 CAPLUS
DOCUMENT NUMBER: 132:306947
TITLE: Japanese encephalitis **DNA vaccine** candidates expressing premembrane and envelope genes induce virus-specific memory B cells and long-lasting antibodies in swine
AUTHOR(S): Konishi, Eiji; Yamaoka, Masaoki; Kurane, Ichiro; Mason, Peter W.
CORPORATE SOURCE: Department of Health Sciences, Kobe University School of Medicine, Kobe, 654-0142, Japan
SOURCE: Virology (2000), 268(1), 49-55
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Swine are an important amplifier of Japanese encephalitis (JE) virus in the paradomestic environment. In this study, two JE **DNA vaccine** candidates were evaluated for immunogenicity in swine. Both vaccine plasmids encode a cassette consisting of the signal of premembrane (prM), prM, and envelope (E) coding regions of JE virus. One plasmid, designated pcJEME, is based on a com. vector (pcDNA3), whereas the other plasmid, designated pNJEME, is based on a vector (pNGVL4a) designed to address some of the safety concerns of **DNA vaccine** use. No differences were detected in the immunogenicity of these two plasmids in mice or swine. Swine immunized with the **DNA vaccines** at a dose of 100 to 450 μg at an interval of 3 wk developed neutralizing and hemagglutination-inhibitory (HAI) antibody titers of 1:40 to 1:160 at 1 wk after the second immunization. However, swine administered two doses of a com. JE vaccine (**formalin**-inactivated virus preparation; JEVAX-A) developed low (1:10) or undetectable antibody responses after their boost. Interestingly, serum antibody titers elicited by **DNA vaccines** in swine were higher than those detected in mice. Eight days after boosting with viral antigen (JEVAX-A) to detect an anamnestic response, swine immunized two times with the **DNA vaccine** showed a >100-fold elevation in HAI titer, indicating a strong recall of antibody response. Swine maintained detectable levels of HAI antibody for at least 245 days after two immunizations with a **DNA vaccine**. These results indicate that these **DNA vaccines** are able to induce virus-specific memory B cells and long-lasting antibodies in swine, which were of higher levels than those obtained with a com. **formalin**-inactivated JE vaccine. (c) 2000

Academic Press.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:72431 CAPLUS
DOCUMENT NUMBER: 132:106589
TITLE: Influenza vaccines: present and future
AUTHOR(S): Subbarao, Kanta
CORPORATE SOURCE: Influenza Branch Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases Centers for Disease Control and Prevention, Atlanta, GA, 30333, USA
SOURCE: Advances in Virus Research (1999), 54, 349-373
CODEN: AVREA8; ISSN: 0065-3527
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 135 refs. on the formulations, clin. results, indications and contraindications of trivalent **formalin**-inactivated influenza vaccines that include influenza A (H3N2), influenza A (H1N1), and influenza B virus components. Similar parameters were also discussed for recombinant and subunit vaccines, as well as live-attenuated influenza vaccines (LAIV), adjuvanted vaccines, cell culture-derived vaccines, **DNA vaccines**, and genetically engineered LAIV. (c) 1999 Academic Press.
REFERENCE COUNT: 137 THERE ARE 137 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:697550 CAPLUS
DOCUMENT NUMBER: 132:34407
TITLE: Evaluation of tick-borne encephalitis **DNA vaccines** in monkeys
AUTHOR(S): Schmaljohn, Connie; Custer, David; VanderZanden, Lorna; Spik, Kristin; Rossi, Cynthia; Bray, Mike
CORPORATE SOURCE: Virology Division, United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD, 21702, USA
SOURCE: Virology (1999), 263(1), 166-174
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tick-borne encephalitis is usually caused by infection with one of two flaviviruses: Russian spring summer encephalitis virus (RSSEV) or Central European encephalitis virus (CEEV). The authors previously demonstrated that gene gun inoculation of mice with naked **DNA vaccines** expressing the prM and E genes of these viruses resulted in long-lived homologous and heterologous protective immunity. To further evaluate these vaccines, the authors inoculated rhesus macaques by gene gun with the RSSEV or CEEV vaccines or with both **DNA vaccines** and compared resulting antibody titers with those obtained by vaccination with a com., **formalin**-inactivated vaccine administered at the human dose. Vaccinations were given at days 0, 30, and 70. All of the vaccines elicited antibodies detected by ELISA and by plaque-reduction neutralization tests. The neutralizing antibody responses persisted for at least 15 wk after the final vaccination. Because monkeys are not uniformly susceptible to tick-borne encephalitis, the protective properties of the vaccines were assessed by passive transfer of monkey sera to mice and subsequent challenge of the mice with RSSEV or CEEV. One hour after transfer, mice that received 50 μl of sera from monkeys vaccinated with both **DNA vaccines**

had circulating neutralizing antibody levels <20-80. All of these mice were protected from challenge with RSSEV or CEEV. Mice that received 10 μl of sera from monkeys vaccinated with the individual **DNA vaccines**, both **DNA vaccines**, or a com. vaccine were partially to completely protected from RSSEV or CEEV challenge. These data suggest that **DNA vaccines** may offer protective immunity to primates similar to that obtained with a com. inactivated-virus vaccine. (c) 1999 Academic Press.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:536210 CAPLUS
DOCUMENT NUMBER: 131:285036
TITLE: Respiratory syncytial virus G and/or SH protein alters Th1 cytokines, natural killer cells, and neutrophils responding to pulmonary infection in BALB/c mice
AUTHOR(S): Tripp, Ralph A.; Moore, Deborah; Jones, Les; Sullender, Wayne; Winter, Jorn; Anderson, Larry J.
CORPORATE SOURCE: Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, National Center of Infectious Diseases, Atlanta, GA, 30333, USA
SOURCE: Journal of Virology (1999), 73(9), 7099-7107
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB BALB/c mice sensitized to vaccinia virus expressed G protein of respiratory syncytial virus (RSV) develop a Th2-type cytokine response and pulmonary eosinophilia when challenged with live RSV. In this study, BALB/c mice were immunized or challenged with an RSV mutant lacking the G and SH proteins or with **DNA vaccines** coding for RSV G or F protein. F or G protein **DNA vaccines** were capable of sensitizing for pulmonary eosinophilia. The absence of the G and/or SH protein in the infecting virus resulted in a consistent increase both in pulmonary natural killer cells and in gamma interferon and tumor necrosis factor expression, as well as, with primary infection, a variable increase in neutrophils and CD11b+ cells. The development of pulmonary eosinophilia in **formalin**-inactivated RSV-vaccinated mice required the presence of the G and/or SH protein in the challenge virus. These data show that G and/or SH protein has a marked impact on the inflammatory and innate immune response to RSV infection.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:644182 CAPLUS
DOCUMENT NUMBER: 130:64888
TITLE: Immunogenicity and efficacy of **DNA vaccines** encoding influenza A proteins in aged mice
AUTHOR(S): Bender, B. S.; Ulmer, J. B.; DeWitt, C. M.; Cottey, R.; Taylor, S. F.; Ward, A. M.; Friedman, A.; Liu, M. A.; Donnelly, J. J.
CORPORATE SOURCE: Department of Medicine, University of Florida College of Medicine, Gainesville, FL, 32610-0277, USA
SOURCE: Vaccine (1998), 16(18), 1748-1755
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Influenza is a leading cause of morbidity and mortality in older persons. The current influenza vaccine is only modestly successful, in part because of an age-related decline in immunogenicity and also because it induces

only type-specified immunity. To overcome this, we evaluated **DNA vaccines** encoding A/PR8/34 hemagglutinin (HA) and nucleoprotein (NP) in young and aged BALB/c mice. Control mice were given **formalin**-inactivated A/PR8/34, control DNA, or a non-LD of PR8. Aged mice given HA DNA developed slightly lower anti-HA serum antibodies than young mice; however, both young and aged mice were protected from a homotypic PR8 challenge. Following vaccination with NP DNA, both young and aged mice developed anti-NP bulk cytotoxic T-lymphocyte (CTL) activity and pCTL frequency similar to control animals. When challenged with a low dose of A/HK/68 (H3N2) influenza virus, both young mice and aged mice showed significant protection as measured by inhibition of weight loss. When challenged with a relatively high dose of A/HR/68 (H3N2) influenza virus, however, the anti-NP vaccine only partially protected young mice and failed to protect aged mice. These data demonstrate that DNA-based vaccines are immunogenic in aged animals, but suggest that factors other than the age-related decline in CTL activity also contribute to the increased morbidity and mortality of influenza in the elderly.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:554628 CAPLUS

DOCUMENT NUMBER: 129:259131

TITLE: Protection against respiratory syncytial virus infection by DNA immunization

AUTHOR(S): Li, Xiaomao; Sambhara, Suryaprakash; Li, Cindy Xin; Ewasyshyn, Mary; Parrington, Mark; Caterini, Judy; James, Olive; Cates, George; Du, Run-Pan; Klein, Michel

CORPORATE SOURCE: Research Centre, Pasteur Merieux Connaught Canada, North York, ON, M2R 3T4, Can.

SOURCE: Journal of Experimental Medicine (1998), 188(4), 681-688
CODEN: JEMEAV; ISSN: 0022-1007

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Respiratory syncytial virus (RSV) remains a major cause of morbidity and mortality in infants and the elderly and is a continuing challenge for vaccine development. A murine T helper cell (Th) type 2 response assocs. with enhanced lung pathol., has been observed in past infant trials using **formalin**-inactivated RSV vaccine. In this study, we have engineered an optimized plasmid DNA vector expressing the RSV fusion (F) protein (DNA-F). DNA-F was as effective as live RSV in mice at inducing neutralizing antibody and cytotoxic T lymphocyte responses, protection against infection, and high mRNA expression of lung interferon γ after viral challenge. Furthermore, a DNA-F boost could switch a preestablished anti-RSV Th2 response towards a Th1 response. Critical elements for the optimization of the plasmid constructs included expression of a secretory form of the F protein and the presence of the rabbit β-globin intron II sequence upstream of the F-encoding sequence. In addition, anti-F systemic immune response profile could be modulated by the route of DNA-F delivery: i.m. immunization resulted in balanced responses, whereas intradermal immunization resulted in a Th2 type of response. Thus, DNA-F immunization may provide a novel and promising RSV vaccination strategy.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:171189 CAPLUS

DOCUMENT NUMBER: 126:210743

TITLE: Characterization of humoral immune responses induced by an influenza hemagglutinin **DNA**

vaccine

AUTHOR(S): Deck, R. Randall; Dewitt, Corrille M.; Donnelly, John J.; Liu, Margaret A.; Ulmer, Jeffrey B.

CORPORATE SOURCE: Merck Research Laboratories, Department of Virus and Cell Biology, West Point, PA, 19486, USA

SOURCE: Vaccine (1997), 15(1), 71-78
CODEN: VACCDE; ISSN: 0264-410X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have examined in detail the characteristics of the humoral immune response and protective efficacy induced by an influenza hemagglutinin (HA) **DNA vaccine**. In mice injected i.m. with HA DNA, the magnitude of the immune responses generated, as measured by ELISA and hemagglutination inhibiting (HI) antibodies, was directly related to the amount of DNA injected and the number of doses administered. The level of anti-HA antibodies in DNA-vaccinated mice was higher than that in convalescent immune mice and was maintained for at least 1.5 yr. The Ig isotype profile of the antibodies was predominantly IgG2a, similar to that induced by live virus infection but in contrast to the relative abundance of IgG1 antibodies observed after inoculation with **formalin**-inactivated whole virus. The presence of pre-challenge HI antibodies was found to be a good correlate of protection, in that every animal with a detectable HI titer was protected from a lethal challenge. Complete protection from a LD of influenza virus (A/PR/34), as judged by 100% survival and no weight loss, was conferred by as little as 1 μg of DNA (given twice). Furthermore, mice injected with 10 to 100 μg doses, when subsequently challenged with virus, showed no increase in HI titer and no production of antibodies directed against the challenge virus, suggesting a substantial inhibition of virus replication after challenge.

L4 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:87817 CAPLUS

DOCUMENT NUMBER: 126:176739

TITLE: Particle-mediated epidermal delivery of DNA and inactivated virus

AUTHOR(S): Justewicz, Dominic M.; Pohlmann, Edward; Sheehy, Michael; Webster, Robert G.

CORPORATE SOURCE: Department of Virology and Molecular Biology, St. Jude Children's Research Hospital, Memphis, TN, 38101, USA

SOURCE: International Congress Series (1996), 1123(Options for the Control of Influenza III), 763-771
CODEN: EXMDA4; ISSN: 0531-5131

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Progress in vaccination is dependent on emerging technologies to maximize antigenicity. A promising candidate is particle-mediated delivery of **DNA vaccines** into the skin. This system was adapted here for the delivery of **formalin**-inactivated virus. Mice were immunized with inactivated virus by "gene gun", and the nature and anatomical localization of the antibody-forming cell (AFC) response examined by enzyme-linked immunospot assay following live virus challenge. Comparison was made with the immunogenicity of adjuvanted **formalin**-inactivated vaccine. Increased nos. of AFCs were generated in lymphoid tissues associated with the respiratory tract by vaccine beads in response to virus challenge, and showed a greater cross-reactive (heterosubtypic) pattern than adjuvanted vaccine. Particle-mediated delivery of inactivated virus shows promise in the development of cross-protective immunity.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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                  (DNA OR DNAS)
L5       128782 4 AND DNA

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         688096 DNA
                  (DNA OR DNAS)
L6       128782 L5 AND DNA

=> formalin and L5
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              2 FORMALINS
          21050 FORMALIN
                  (FORMALIN OR FORMALINS)
L7          273 FORMALIN AND L5

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L8          273 DNA AND L7

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         12078 DAMAGES
        308513 DAMAGE
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         34217 DNA (S) DAMAGE
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            2 FORMALINS
        21050 FORMALIN
                  (FORMALIN OR FORMALINS)
L11          9 FORMALIN AND L10

=> D L11 IBIB ABS 1-9

L11  ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:270287  CAPLUS
DOCUMENT NUMBER:          141:1938
TITLE:                    In vitro mutation artifacts after formalin
                          fixation and error prone translesion synthesis during
                          PCR
AUTHOR(S):                Quach, Nancy; Myron, Goodman F.; Shibata, Darryl
CORPORATE SOURCE:         Department of Pathology, University of Southern
                          California Keck School of Medicine, Los Angeles, CA,
                          USA
SOURCE:                   BMC Clinical Pathology (2004), 4, No pp. given
                          CODEN: BCPMB3; ISSN: 1472-6890
                          URL: http://www.biomedcentral.com/1472-6890/4
PUBLISHER:                BioMed Central Ltd.
DOCUMENT TYPE:            Journal; (online computer file)
LANGUAGE:                 English
AB   Clin. specimens are routinely fixed in 10% buffered formalin and
     paraffin embedded.  Although DNA is commonly extracted from fixed
     tissues and amplified by PCR, the effects of formalin fixation
     are relatively unknown.  Formalin fixation is known to impair
     PCR, presumably through damage that blocks polymerase elongation, but an
     insidious possibility is error prone translesion synthesis across sites of
     damage, producing in vitro artifactual mutations during PCR.  To better
     understand the consequences of fixation, DNA specimens extracted
     from fresh or fixed tissues were amplified with Taq DNA
     polymerase, and their PCR products were cloned and sequenced.
     Significantly more (3- to 4-fold) mutations were observed with
     fixed DNA specimens.  The majority of mutations were
     transitions, predominantly at A:T base pairs, randomly distributed along
     the template.  Formalin fixation appears to cause random base
     damage, which can be bridged during PCR by Taq DNA
     polymerase through error prone translesion synthesis.  Fixed DNA
     is a damaged but "readable" template.
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